A UK Perspective:

PAE: Is It Ready for Prime Time?

A look at the current use of prostate artery embolization for symptomatic benign prostatic hypertrophy and what further dissemination could offer to patients.

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Prostate artery embolization (PAE) for symptomatic benign prostatic hypertrophy was first described in 2000[1] and has attracted much interest in the interventional radiology (IR) and urology worlds. Initial small series have been followed by much larger single-center cohort studies with follow-up out to 7 years. There have also been three randomized controlled trials (RCTs) published from China, Brazil, and Spain.[2-4] Other RCTs are recruiting and should report findings over the next few years.

PAE GUIDELINES AND THE UK-ROPE REGISTRY STUDY

Various countries have issued guidelines concerning PAE. In the United States, the American Urological Association updated its treatment for lower urinary tract symptoms (LUTS) guidelines in 2014,[5] and these did not include PAE. Similarly, the current European Association of Urology guidelines[6] do not include PAE as a treatment option. In Australia and New Zealand, PAE can only be offered in the setting of an approved clinical trial.

In the United Kingdom (UK), the National Institute for Health and Care Excellence (NICE) issued guidelines in 2013, again suggesting that evidence for PAE was insufficient for it to be approved for routine use.[7] However, they did approve PAE within research studies or a well-organized multidisciplinary registry. I was invited to chair a steering committee and initiate such a registry. Funding was provided from industry (via a Cook Medical research grant) and from the British Society of Interventional Radiology and British Association of Urological Surgeons. NICE also provided funding for an independent medical assessment organization (Cedar) to sponsor and run the registry.

The first multicenter prospective registry, UK-ROPE, was initiated in 2014 and completed its recruitment target by January 2016. One-year follow-up data were available by the close of the study at the end of January 2017.[8,9] The primary endpoint was the 12-month International Prostate Symptom Score (IPSS), and there were multiple secondary endpoints such as length of hospital stay, complications, reintervention rates, prostate volumes, flow, and MRI findings.

A total of 305 patients (PAE, 216; transurethral resection of the prostate [TURP], 89) were recruited from 17 centers and followed out to 12 months postprocedure. PAE produced a median 10-point reduction in the IPSS at 12 months with no significant complications. On a 6-point quality-of-life scale, there was a 3-point reduction with PAE compared with 4 points after TURP. Erectile function, as measured by the International Index of Erectile Function short form, showed a slight improvement in both groups.

Urinary flow was measured as Qmax and improved by 3 mL/s compared with 7.5 mL/s after TURP. Median prostate volume was reduced by 28% after PAE. There was also a significant reduction in hospital stay. Over 70% of PAE cases were performed as a same-day discharge, whereas 30% of TURP patients spent 1 night in hospital and 49% spent 2 nights. A few patients needed even longer stays.

High procedural radiation doses have been reported with PAE and this is often noted by urologists criticizing the procedure. In the UK-ROPE study, the median screening time was 38 minutes, with a median dose

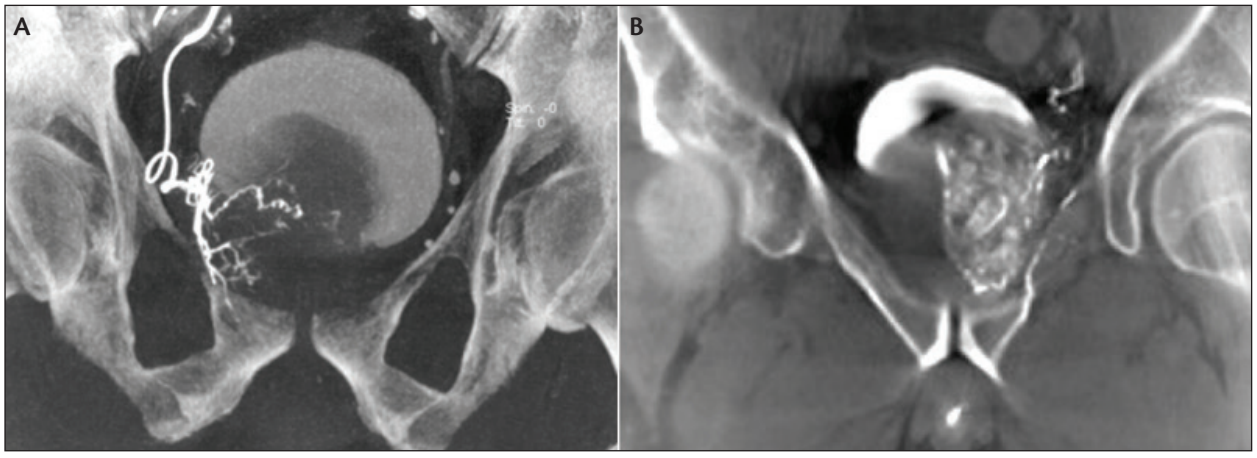

Figure 1. CBCT maximum intensity projection showing a type III origin prostate artery off the obturator on the right (A). Left lobe of the prostate on a 3-mm-slice thickness multiplanar reconstruction CT–like image after superselective left prostate artery injection (B).

area product of 17,892 cGy•cm^2 and median skin dose of 1,368 mGy. There was a learning curve observed, with doses significantly reducing after the first 10 cases in each center as they acquired experience after the initial proctoring period. The routine use of cone-beam CT (CBCT) was encouraged to increase confidence during superselective embolization and reduce the risk of nontarget embolization (Figure 1).

Complications reported were few and categorized as grade I–II on the Clavien-Dindo classification system. After PAE, 18% of patients reported a degree of hematuria, however light, which was less than after TURP (64%). Hematospermia was reported in 12.6%, and patients should be warned about this after PAE. There was one urinary tract infection compared with two in the TURP cohort and four groin hematomas, one requiring drainage and blood transfusion after failure of a closure device.

Because there is minimal blood loss after PAE, it is not contraindicated in patients with anemia or clotting disorders or those on anticoagulant therapy. Erectile function did not worsen after PAE or TURP and, in fact, slightly improved in both groups. Retrograde ejaculation (RE) was reported only half as often after PAE (24%) compared with TURP (48%). It is likely that this difference was probably underestimated due to the patients' embarrassment during the self-reporting process (only 61/89 replies in TURP group) and due to the presence of preexisting RE in the PAE group after previously commencing α-blockers.

There were two cases of self-limiting penile ulceration, but no other reported nontarget embolizations.

Although not quite as effective as TURP in this cohort (15-point IPSS reduction), it was concluded that PAE is very effective at reducing symptom scores, and due to its good safety profile, it is worth considering in men who want to avoid TURP and the inevitable side effects associated with it.

UK-ROPE had many strengths. Although not an RCT, it was multidisciplinary and multicenter. It had a noninferiority design (compared with TURP) and was run by an independent medical assessment unit and not by IRs or urologists who might have introduced bias into the results. The report was instigated by NICE, the medical regulatory authority that insisted on the highest standards. NICE was the first to receive the report, which, along with the other published data on PAE, provides a firsthand understanding of the procedure.

Subgroup analysis is ongoing, but it was of note that centers performing only 10 to 15 cases had results as good as the highest recruiting centers performing more that 40 cases. Radiation doses were shown to markedly decrease as experience increased.

A team approach was mandatory in this study. All actively involved units had to include two urologists and two IRs. All centers visited a training center in Europe or the UK, and all had in-house proctoring for at least the first four cases.

All published series to date have shown nearly the same results.[10] Some further improvement has been reported by Carnevale et al using the "PErFecTED" technique, and where possible, this does appear to cause more glandular infarction, which should provide longer-lasting symptomatic improvement.[11] Care must

be taken with overall radiation doses in all cases using the PErFecTED technique.

OBSTACLES TO WIDESPREAD IMPLEMENTATION OF PAE

National and international guidelines need to be updated to include PAE as a treatment option for men with enlarged, symptomatic prostates with no evidence of malignancy who would like to avoid conventional or laser prostatectomy. If national or international urologic institutions are not convinced by the current level of data and likely NICE approval in the UK, then a large-scale, multicenter, multinational registry or even RCT should be performed, as there is much enthusiasm for this within the IR and urology communities.

Urologists need to be convinced that rather than competing for patients, IRs are providing a very effective, even if only temporary, solution to men who would like to avoid or at least delay surgery if possible. Far from reducing a urologist's practice, it actually increases it, as only a proportion of men presenting with LUTS will, after appropriate investigation, be suitable for PAE, either alone or followed by interval median lobe resection.

Reimbursement codes and tariffs will need to reflect the complex nature of PAE and the high cost of consumables, which can be weighed against the fact that PAE can be performed on an outpatient or same-day discharge basis.

TRAINING AND PROCTORING

PAE is a complex interventional procedure fraught with potential complications for the inexperienced operator. IRs performing large numbers of embolizations, particularly when requiring microcatheters, are the ideal physicians to offer PAE. With proper equipment, training, and proctoring, most will be able to provide a very safe and effective service.

The variable and at first glance complex anatomic variations of prostatic arterial supply can readily be learned at training courses and at a physician's base hospital by using a clear anatomic template and applying the five types and origins of the prostatic artery.[12]

Suitably qualified IRs who have attended a PAE training course at an approved center can usually learn to safely perform PAE after two proctored sessions with a minimum of two cases per session.

CONCLUSION

In my view, PAE is now ready for prime time. The initial report from UK-ROPE has just been accepted for publication in *British Journal of Urology International,* and as of this writing, NICE is due to issue further guidelines on PAE on April 25, 2018. If, as I hope, PAE gets approval for use in the UK, then I have little doubt that it will spread rapidly here. Many other countries use NICE guidelines as well, but may still insist on further evidence. That remains to be seen. ■

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